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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/616,448

07/08/2003

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0103.11

1036

21968 7590 11/14/2008
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EXAMINER

ARNOLD, ERNST V

ART UNIT

PAPER NUMBER

1616

MAIL DATE

DELIVERY MODE

11/14/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

DETAILED ACTION

Claims 1, 3-5, 11-15 and 21-34 are pending and under examination.

Withdrawn rejections:

Applicant's amendments and arguments filed 9/16/08 are acknowledged and have been fully considered. Any rejection and/or objection not specifically addressed below is herein withdrawn.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1, 3-5, 11-15 and 21-34 remain/are rejected under 35 U.S.C. 103(a) as being unpatentable over Schulz et al. (US 6,116,237) in view of Hanes et al. (US 5,855,913) and Radhakrishnan (US 5,049,389).

Applicant claims a method for the pulmonary administration of a dry powder composition.

Determination of the scope and content of the prior art

(MPEP 2141.01)

Schulz et al. teach in claims 1-12 methods for inhalation of dry powder drug. The drug composition can have an inert carrier column 3, lines 65-67 and claim 7). Claim 12 is reproduced below:

12. A method for inhalation of a dry powder drug, comprising the steps of:

- a) providing a dry powder drug composition having a drug particle size of from about 1–7 microns and mass median aerodynamic diameter of the delivered aerosol of from about 3 to 6 microns;
- b) loading the dry powder drug composition into an inhaler which is generally flow rate independent, and with the inhaler having an inspiration flow resistance of about 0.12 to 0.21 (cm H₂O)^{1/2} over the range of about 10–60 L/min;
- c) inhaling the drug composition from the inhaler with an inspiration flow rate of about 15–60 L/min, resulting in a delivery efficiency measured by respirable fraction of at least 20%.

Hanes et al. teach in claim 1:

1. A particulate composition for drug delivery to the pulmonary system comprising:

biodegradable particles incorporating a therapeutic, prophylactic or diagnostic agent and a surfactant, wherein the particles have a tap density less than 0.4 g/cm³ and a mean diameter between 5 μm and 30 μm effective to yield an aerodynamic diameter of the particles of between approximately one and three microns.

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Hanes et al. teach phospholipids as the surfactant in claims 14-17:

14. The composition of claim 1 wherein the surfactant is selected from the group consisting of a fatty acid, a phospholipid, and a poloxamer.

15. The composition of claim 1 wherein the surfactant is a phosphoglyceride.

16. The composition of claim 1 wherein the surfactant is dipalmitoyl L- α -phosphatidylcholine.

Hanes et al. teach any surfactant known in the art can work in column 5, lines 39-47:

Surfactants known in the art can be used including any naturally occurring lung surfactant. Other exemplary surfactants include diphosphatidyl glycerol (DPPG); hexadecanol; fatty alcohols such as polyethylene glycol (PEG); polyoxyethylene-9-lauryl ether; a surface active fatty acid, such as palmitic acid or oleic acid; sorbitan trioleate (Span 85); glycocholate; surfactin; a poloxomer; a sorbitan fatty acid ester such as sorbitan trioleate; tyloxapol and a phospholipid.

Hanes et al. teach porous microparticles (column 16, lines 25-35, for example).

Hanes et al. teach a wide variety of therapeutic agents including parathyroid hormone and leuprolide (column 10, lines 37-49 and claim 25).

Radhakrishnan teach inhalation method for treatment of lung diseases with tobramycin and other actives (claims 13, 15, 18 and 20).

Ascertainment of the difference between the prior art and the claims

(MPEP 2141.02)

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1. The difference between the instant application and Schulz et al. is that Schulz et al. do not expressly teach a lipid matrix that comprises phospholipids or hollow porous microparticles. This deficiency in Schulz et al. is cured by the teachings of Hanes et al.

2. The difference between the instant application and Schulz et al. is that Schulz et al. do not expressly teach an active agent selected from the group consisting of budesonide, tobramycin sulfate, leuprolide acetate, amphotericin B and parathyroid hormone. This deficiency in Schulz et al. is cured by the teachings of Hanes et al. and Radhakrishnan.

Finding of prima facie obviousness

Rational and Motivation (MPEP 2142-2143)

1. It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to use hollow porous phospholipid inert carriers in the method of Schulz et al., as suggested by Hanes et al., and produce the instant invention.

One of ordinary skill in the art would have been motivated to do this because: 1) Schulz et al. do not specify the type of drug carrier and Hanes et al. provide the nexus teaching to use phospholipids and 2) Hanes teaches that porosity affects the tap density which in turn regulates the aerodynamics and increasing porosity permits delivery of larger particle envelope volumes into the lungs (column 9, lines 2-12 and 19-25 and

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general discussions in this column), which is a desirable feature with inhaled medications.

With regard to the Anderson Cascade Impaction or multi-stage liquid impinger limitations, it is the Examiner's position that the art used an equivalent method to arrive with values within the instantly claimed range. Lung deposition amounts are merely a matter of routine optimization of the amounts taught by Schulz et al.

2. It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to select actives from the group consisting of budesonide, tobramycin sulfate, leuprolide acetate, amphotericin B and parathyroid hormone in the method of Schulz et al., as suggested by Hanes et al. and Radhakrishnan, and produce the instant invention.

One of ordinary skill in the art would have been motivated to do this because these actives are taught for pulmonary administration. Selection of the sulfate salt of tobramycin is merely a matter of judicious selection by one of ordinary skill in the art.

A reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill in the art might reasonably infer from the teachings. (*In re Opprecht* 12 USPQ 2d 1235, 1236 (Fed Cir. 1989); *In re Bode* 193 USPQ 12 (CCPA) 1976).

In light of the forgoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a).

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From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Response to arguments:

Applicant asserts that the primary reference does not teach a passive dry powder inhaler and therefore the Examiner has failed to establish a *prima facie* case. Applicant states: "a "passive dry powder inhaler" refers to an inhalation device which relies on the patient's inspiratory effort to disperse and aerosolize a drug formulation." (Remarks page 1). The primary reference of Schulze et al. above clearly relies on the patient's inspiratory effort to disperse and aerosolize a drug formulation. Schulze et al. teach in the Abstract (examiner added emphasis):

A method for inhalation of a dry powder drug includes the steps of providing a dry powder drug composition having a drug particle size of from about 1-7 microns and a mass median aerodynamic diameter of the delivered aerosol of from about 3.5 to 5.5 microns. This composition is loaded into an inhaler which is generally flow rate independent, and with the inhaler having an inspiration flow resistance of about 0.12 to 0.21 (cmH₂O)^{1/2} over the range of about 15-60 L/min. The patient inhales the drug composition from the inhaler with an inspiration flow rate of about 15-60 L/min, resulting in a delivery efficiency measured by respirable fraction greater than 20%.

The Examiner also directs Applicant to column 6, lines 17-58 with lines 17-18 reproduced below to show that the patient drives the device by inhalation:

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The mouthpiece 209 is placed into the user's mouth. As the user gently inhales, a slight pressure drop is created in

The device of Schulze et al. is passive by Applicant's own definition. Applicant asserts that their definition excludes devices that require means providing energy to disperse and aerosolize the drug formulation. The claim language of Schulze et al. does not positively recite that means providing energy to disperse and aerosolize the drug formulation are required. While Schulze et al. disclose an embodiment that does require a motor and impeller, the claim language of Schulze et al. is broader in scope and encompasses those devices which do not require such means. Schulze et al. clearly describe an inhaler that has all the functional properties instantly claimed. Therefore, the Examiner concludes that Applicant's invention remains obvious over Schulze et al. The art already teaches powder inhaler devices that meet Applicant's specifications and the art teaches the types of powder actives to use in powder inhalers. What is unexpected about putting a powder for inhalers into an inhaler for that purpose? Applicant's following arguments are not persuasive and the rejection is maintained.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422

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F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 3-5, 11-15 and 21-34 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 44-48 and 51-53 of copending Application No. 09/851,226 in view of (US 6,116,237) and Hanes et al. (US 5,855,913). The copending application teaches methods of delivering an active agent to the respiratory tract of the patient with particles having a mass median diameter of less than 20 microns; an aerodynamic diameter of less than 10 microns; a bulk density of less than 0.5 g/cm³; the active can be tobramycin and the particles are hollow and porous. The copending application does not expressly disclose the resistance of the dry powder inhaler or hollow porous particles. This deficiency is cured by the teachings of Schulz et al. and Hanes et al. which are discussed in detail above and those discussions are hereby incorporated by reference. One of ordinary skill in the art would have recognized the obvious variation of the instant invention over the copending application and Schulz et al. and Hanes et al. and would have had a reasonable expectation of success using the inhaler of Schulz et al.

Claims 1, 3-5, 11-15 and 21-34 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 4-7, 22 and 36-38 of copending Application No. 10/141,219 (now revived) in view of (US

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6,116,237). The copending application teaches methods for administering a dry powder composition comprised of leupolide and phospholipid with a median diameter of between 0.5-4 microns, aerodynamic diameter of less than 5 microns, bulk density of about 0.5 g/cm³, dry powder inhaler, emitted dosages, and various phospholipids. The copending application does not expressly disclose the resistance of the dry powder inhaler or hollow porous particles. This deficiency is cured by the teachings of Schulz et al. and Hanes et al. which are discussed in detail above and those discussions are hereby incorporated by reference. One of ordinary skill in the art would have recognized the obvious variation of the instant invention over the copending application and Schulz et al. and Hanes et al. and would have had a reasonable expectation of success using the inhaler of Schulz et al.

Claims 1, 3-5, 11-15 and 21-34 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 23-25, 29 and 30 of copending Application No. 11/187,757 in view of (US 6,116,237). The copending application is drawn to methods for treating a patient comprising administering particulates via inhalation having a mass median diameter of less than 20 microns, lipid matrix, amphotericin B, and a geometric diameter of less than 3 microns. The copending application does not expressly disclose the resistance of the dry powder inhaler or hollow porous particles. This deficiency is cured by the teachings of Schulz et al. and Hanes et al. which are discussed in detail above and those discussions are hereby incorporated by reference. One of ordinary skill in the art would have recognized the obvious variation of the instant invention over the copending application and Schulz

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et al. and Hanes et al. and would have had a reasonable expectation of success using the inhaler of Schulz et al.

This is a provisional obviousness-type double patenting rejection.

Claims 1, 3-5, 11-15 and 21-34 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-4, 6-15, 17-19, 21-24, 26-34, 36-38, and 39-57 of U.S. Patent No. 7,306,787 in view of US 6,116,237. The patented claims are drawn to a method of delivering a therapeutic dose of a bioactive agent to the pulmonary air passages. Phospholipids and actives as instantly claimed are taught. The US Patent does not expressly disclose the resistance of the dry powder inhaler or hollow porous particles. This deficiency is cured by the teachings of Schulz et al. and Hanes et al. which are discussed in detail above and those discussions are hereby incorporated by reference. One of ordinary skill in the art would have recognized the obvious variation of the instant invention over the patented claims and Schulz et al. and Hanes et al. and would have had a reasonable expectation of success using the inhaler of Schulz et al.

Response to arguments:

Applicant's arguments are not persuasive for the reasons given above. The rejections are maintained.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ernst V. Arnold whose telephone number is 571-272-8509. The examiner can normally be reached on M-F (6:15 am-3:45 pm).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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